

PATENT SPECIFICATION

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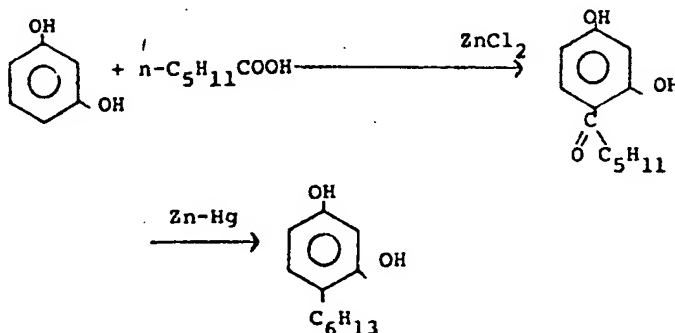


(54) ALKYLATION OF AROMATIC HYDROXY COMPOUNDS

(71) We, CONOCO INC. formerly Continental Oil Company, a corporation organized and existing under the laws of the State of Delaware, United States of America, located at 1000 South Pine Street, Ponca City, Oklahoma 74601, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to the liquid phase alkylation of hydroxy aromatic components to produce n-alkylated cresylic acids by contacting a cresylic acid with an n-alkanol. For example, this invention enables the production of n-hexyl resorcinol by direct alkylation of resorcinol under liquid phase conditions.

Many commercial applications exist for n-alkylated cresylics. For example, 4-n-hexyl resorcinol is an antiseptic and an anthelmintic. This particular compound is commonly prepared by condensing hexanoic acid with resorcinol and reducing the resulting ketone using a mercury-zinc amalgam. The prior art reaction is shown in Equation I.



The condensation step encountered in the prior art is not exceedingly difficult, although a glass-lined reactor is normally required because of the zinc chloride involved. The zinc chloride can be regenerated and reused. The main problem with the prior art procedure arises from the reduction using a zinc-mercury amalgam because of mercury contamination problems. These contamination problems, combined with the exceedingly high cost of the zinc-mercury amalgam, contribute to the high cost of this 4-hexyl resorcinol.

It would therefore be distinctly advantageous to provide a process for the production of compounds such as n-hexyl resorcinol using a method which does not involve the expensive zinc-mercury amalgam with its attendant contamination problems nor the condensation in the presence of toxic zinc chloride, requiring glass-lined reactors and recovery of materials, and to produce primarily an n-alkylated side chain. Previous attempts to directly alkylate resorcinol such as described in U.S. Patent 2,448,942, produced not n-hexyl resorcinol, but isohexyl resorcinol, which does not have the properties necessary to act as an antiseptic and anthelmintic in humans.

In one aspect our invention provides a method for the production of an alkylated phenolic product containing predominantly n-alkylated side chains which

comprises directly alkylating a phenolic compound selected from resorcinol, phenol, isomerized xylenols, hydroquinone, o-cresol, p-cresol and m-cresol with an n-alkanol having from 4 to 10 carbon atoms, at pressures up to 20 atmospheres and temperatures of from 200° to 400°C in the presence of an alumina catalyst derived from aluminum alkoxide hydrolysis.

According to the present invention the direct alkylation process can utilize pressures of e.g. from atmospheric pressure to 1,000 pounds per square inch gauge (psig). In some reactions, the presence of water is found to be helpful. If water is not present, reaction temperatures are often from 330°C to 340°C. Normally, from 0.1 to 1 mole of water per mole of cresylic acid (i.e. a phenolic compound as defined above) will be used. However, from 0.4 to 0.6 mole is preferred.

Alcohols useful in the practice of the present invention are n-alcohols containing from 4 to 10 carbon atoms. Representative examples of such alkanols are n-butanol, n-pentanol, n-hexanol, n-heptanol, n-octanol, n-nonanol, and n-decanol.

Cresylic acids useful in the practice of the present invention are phenol, o-cresol, p-cresol, m-cresol, isomeric xylenols, hydroquinone, and resorcinol. Mixtures of any of these can also be used.

The most preferred compound produced by the practice of the present invention is n-hexyl resorcinol because of its large commercial market and antiseptic properties. However, it should be understood that the process of the present invention is effective to prepare other n-alkylated cresylic acids as well. The process of the present invention allows direct alkylation of the cresylic rings without excessive isomerization of the alkyl moiety.

Catalysts useful in the present invention are alumina catalysts derived from aluminum alkoxide hydrolysis. Representative examples of such aluminas are Catapal and Dispal aluminas, trademarks of and sold by Continental Oil Company. When these aluminas are used as catalysts, lower and temperatures can be used than when aluminas from other sources are used. Normally these aluminas used in this invention allow reactions to occur at temperatures of from 230 to 300°C and pressures of 1—20 atmospheres together with continuous removal of water. These decreased temperatures and pressures allow still less isomerization of side chains than found with alumina catalysts generally and magnesium oxide catalysts, and the invention is a great improvement over the prior art processes where primarily side-chain isomerization was found.

Although the reaction can be carried out either batchwise or continuously, continuous reactions are preferred. When carried out continuously, liquid hourly space velocities may e.g. be from 0.01 to 30, but from 0.1 to 3 is preferred.

The invention will now be illustrated with reference to the Examples below wherein all parts and percentages are by weight unless otherwise specified. The Examples should be construed to exemplify the present invention and in no way limit it. Example 7 is given for comparison.

Example 1

An electrically heated 1/2-inch diameter stainless steel tube containing 15 milliliters of Catapal SB alumina extrudate was used as a reactor. All reactants were pumped through a preheater into the reactor and were cooled before exiting through a back pressure regulator maintaining a system pressure of 300 pounds per square inch gauge. The feed composition was 1 mol of resorcinol (110.1 grams), 0.4 mole of n-hexanol (40.8 grams), and 0.5 mole of water (9.0 grams). A reaction temperature of between 340 and 360°C was investigated. Conversion increased with temperature, and selectivity to the desired products remained nearly constant. The major products were n-hexyl resorcinol, the n-hexyl ether of resorcinol, and isohexyl resorcinol. The ether was recycled. The ratio of normal to isohexyl resorcinol product was 70 to 30, respectively.

Example 2

A reaction is carried out as described in Example 1 except that water is excluded from the feed composition. At the temperature used, the product composition and distribution is nearly the same even in the absence of water.

The following Examples illustrate the effectiveness of aluminas derived from aluminum alkoxide hydrolysis. Aluminas used were Catapal® SB alumina, except for Example 7, which used Alcoa FI Alumina and is inserted for comparative purposes.

Example 3

In a 500 ml flask fitted with thermometer, mechanical stirrer, addition funnel, and a Dean-Stark trap, with attached condenser is placed 110 g of resorcinol and 71.4 g of 1-hexanol. The reaction mixture was heated at 160–200°C for 4 hours with no apparent reaction taking place. Alumina (15 g) was added and the mixture heated gradually to 255°C over a period of 4 hours, 1.8 ml of water having been produced. Hexanol was removed from the reaction by drawing off through the Dean-Stark trap to allow the temperature to reach 255°C. Refluxing was continued at 240–255°C with the reflux temperature being controlled by the periodic addition of hexanol (that which had been removed) back to the reaction mixture. This procedure was continued over a period of about 8 hours, during which time all of the original hexanol had been added back to the reaction mixture, and during which 16.7 ml of produced water had been collected in the Dean-Stark trap. The reaction mixture was analyzed at this point (using o-cresol as an external standard) and was found to have the following composition, as determined by area under a gas chromatograph curve.

		Area %	
	Hexenes	2.25	
	1-hexanol	7.31	
20	Resorcinol	16.23	20
	Monohexylether of Resorcinol	3.37	
	2-n-hexylresorcinol	1.93	
	4-n-hexylresorcinol	18.93	
	Sec-hexylresorcinol	1.82	
25	Dihexylresorcinols	8.89	25
	Non-Eluting Material	39.27	

A part of the crude reaction product (ca 90 g) was taken up in 500 ml of diisopropyl ether and washed with one 300 ml portion of 1N sulfuric acid and then with five 300 ml portions of water. The combined aqueous phases were back-extracted with 100 ml of diisopropyl ether, and this was combined with the other organic phase. Isopropyl ether was mostly removed from the organic material on a rotary evaporator. The residue 142 g was charged to a 4-foot spinning band fractional distillation column and distilled, the results shown in Table 1.

TABLE 1

Cut No.	b.p.	wt. g.
1	50–71° 1 atm.	67.0 g
2	48–138° 2 torr	9.6 g
3	142–162° 2 torr	9.1 g
4	174–176° 2 torr	20.2 g
5	176–219° 2 torr	8.3 g
Residue	—	17.4 g
Trap	—	2.0 g
Loss and Hold-up	—	8.8 g

The individual cuts were analyzed by gas chromatography. Cut 1 was essentially pure diisopropyl ether with about 8 percent hexenes. The compositions of the other cuts are listed in Table 2.

TABLE 2
Analysis of Distillation Cuts

Component	Area % of Cut				Total wt, Grams
	2	3	4	5	
Hexanol	53.92	0.52	—	—	5.22
Resorcinol	31.62	38.98	0.52	—	6.58
Mono-n-hexylethyl of resorcinol	3.10	24.70	2.58	0.99	3.15
2-n-hexylresorcinol	0.11	7.05	4.05	1.18	1.56
4-n-hexylresorcinol	0.10	3.47	84.62	14.17	18.60
Sec-hexylresorcinols	—	0.54	5.47	10.61	2.03
Dihexylresorcinols	—	—	2.10	64.00	5.73
Others	11.15	24.74	0.66	9.05	—

The isolated yield of 4-n-hexylresorcinol amounts to about 24 wt %.

A portion of cut 4, 5 g. was recrystallized from petroleum ether to yield light yellow platelets, m.p. 57°C (m.p. of 4-n-hexylresorcinol is 61°C). The proton magnetic resonance spectrum of the recrystallized material was identical with that of a known sample of 4-n-hexylresorcinol.

Example 4

The reaction of 1-hexanol with resorcinol over alumina was repeated, except that samples of the reaction mixture were removed at various conversion levels and analyzed. Thus, to a mixture of 110 g (1.0 mole) of resorcinol and 20 g of calcined powdered Catapal SB alumina, heated to 255°C, was added 102 g (1.0 mole) of 1-hexanol at such a rate as to maintain the temperature at 250–260°C (about 8–10 hours) with vigorous reflux. Samples of the reaction mixture were removed as follows:

Reaction Time Hours	ml of Water Produced	Sample No.
3	7	1
5	10	2
7	14	3
10	18	4
14	22	5

These samples were weighed into a weighed amount of m-cresol (used as an external gas chromatography standard) and analyzed on a 10'x1/8" SE-30 gas chromatography column programmed from 100 to 350°C at 10° per minute. Results of these analyses are listed in Table 3.

TABLE 3

Analysis of Samples from Example 5

Component	Percent, in Sample No.				
	1	2	3	4	5
1-Hexanol	14.48	6.44	6.42	12.97	3.57
Resorcinol	46.77	28.03	19.40	9.68	4.83
Light Unknowns	2.57	2.67	2.12	2.42	1.13
Hexyl Resorcy Ether	4.66	4.12	4.19	3.46	3.31
2-n-hexylresorcinol	1.63	1.59	2.04	1.64	2.82
4-n-hexylresorcinol	9.61	16.87	20.74	18.81	15.86
Sec-hexylresorcinols	3.26	0.76	3.18	*	1.71
Di- & trihexylresorcinols	4.23	5.80	12.21	*	*
Non-Eluting Material	12.79	33.72	29.70	51.02	66.77

* These components were not well analyzed. They are lumped into the non-eluting material figure.

The data of Table 3 allows conversions and selectivities to be calculated, where weight percent selectivity is defined as the percent of 4-n-hexylresorcinol x 100/wt % of all components except water, unreacted hexanol, unreacted resorcinol, and hexyl resorcy ether.

	Sample No.				
	1	2	3	4	5
Approximate Wt % Conversion of Resorcinol	42.6	57.8	66.9	81.5	90.8
Wt % Selectivity to 4-n-Hexylresorcinol	14.6	27.5	29.6	25.5	18.0

Example 5

The reaction of Example 3 is repeated, except that it is conducted in an autoclave wherein the pressure may be maintained at 75 psig. 1-hexanol is fed into the reactor by a pump, which, in turn, is controlled by a temperature actuated switch, so that as the temperature reaches 250°C, hexanol is pumped in until the reflux temperature drops to just below 250°C. As the hexanol is consumed, and the water removed via the trap, the temperature rises to just above 350°C whereupon the pump is again actuated and more hexanol added. In this way, the steady-state concentration of hexanol in the reaction mixture is increased.

Example 6

4-n-octyl resorcinol is prepared by heating 1-octanol with resorcinol in the presence of 20 wt % alumina. The 1-octanol is added at such a rate that the temperature is maintained at 275°C, with continuous removal of the water formed.

Example 7 (comparative)

The reaction of 1-hexanol and resorcinol, as conducted in Example 3, was repeated except that the alumina used was Alcoa F1 alumina, (derived from sodium aluminate) rather than Catapal® alumina. No 4-n-hexylresorcinol production was observed.

It will be apparent from the process described herein that a much improved process is provided for the preparation of n-alkylated cresylic acids. The use of toxic, expensive, and corrosive materials such as zinc chloride for condensation is avoided as is the use of an expensive and polluting zinc-mercury amalgam. The process of the instant invention consists of but a single step and can be carried out in a continuous reactor to produce a mixture containing the products desired.

While certain embodiments and details have been shown for the purpose of illustrating this invention, it will be apparent to those skilled in the art that various changes and modifications may be made herein without departing from the scope of the invention.

WHAT WE CLAIM IS:—

1. A method for the production of an alkylated phenolic product containing predominantly n-alkylated side chains which comprises directly alkylating a phenolic compound selected from resorcinol, phenol, isomerized xylenols, hydroquinone, o-cresol, p-cresol and m-cresol with an n-alkanol having from 4 to 10 carbon atoms, at pressures up to 20 atmospheres and temperatures of from 200° to 400°C in the presence of an alumina catalyst derived from aluminum alkoxide hydrolysis.

2. A method according to claim 1, wherein the reaction mixture in addition contains water at a level of from 0.1 to 1 mole per mole of said phenolic compound.

3. A method as claimed in claim 2, wherein from 0.4 to 0.6 mole of water is employed per mole of said phenolic compound.

4. A method as claimed in any of the preceding claims, wherein the reaction is carried out in a continuous reactor.

5. A method as claimed in any of the preceding claims, wherein said phenolic compound is resorcinol and said n-alkanol is n-hexanol.

6. A method as claimed in any of the preceding claims, wherein the reaction is carried out at temperatures of from 230 to 300°C.

7. A method according to claim 1, wherein the reaction temperature is from 230 to 300°C and wherein water is continuously removed from the reaction as it is formed.

8. A method as claimed in claim 7, wherein the n-alkanol is n-hexanol.

9. A method according to claim 1, substantially as described herein.

10. A method according to claim 1, substantially as described herein with reference to any one of Examples 1—6.

11. Alkylated phenolic products when prepared by the process of any of the preceding claims.

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